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Ref. No. 27712 (formerly 01337.US1)

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Canceled)

2. (Previously Presented) The method of claim 20, wherein each  $R^4$  is independently

- (a) H,
- (b) halo,
- (c)  $SR^{12}$ ,
- (f)  $S(O)_mR^{13}$ ,
- (g)  $NR^9R^{10}$ ,
- (h)  $NR^9S(O)_mR^{13}$ ,
- (i)  $NR^9C(=O)OR^{13}$ ,
- (j) phenyl optionally substituted by one or more  $R^8$ ,
- (k) heteroaryl optionally substituted by one or more  $R^8$ ,
- (l) cyano,
- (m) nitro,
- (n)  $CONR^9R^{10}$ ,
- (o)  $CO_2R^{12}$ ,
- (p)  $C(=O)R^{13}$ ,
- (q)  $C(=NOR^{12})R^{13}$ ,
- (s)  $NR^9C(=O)-R^{12}$ ,
- (t)  $C_{1-7}$ alkyl,  $C_{1-7}$  alkenyl or  $C_{1-7}$  alkynyl each of which is optionally substituted by one or more  $R^{11}$ , or
- (u)  $het^1$  optionally substituted by one or more  $R^8$ .

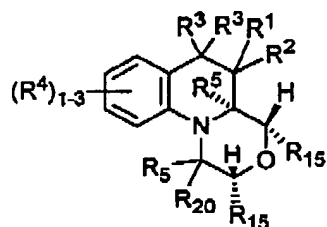
3. (Previously Presented) The method of claim 2, wherein each  $R^4$  is independently selected from  $NO_2$ , H, Br, F,  $CF_3$ , CN,  $NH_2$ ,  $-C(O)-OCH_3$ ,  $-S-CH_3$ ,  $-S(O)_2-CH_3$ ,  $-N(OCH_3)-CH_3$ ,  $-NH-C(O)-O-tbutyl$ ,  $-NH-C(O)-CH_3$ , heteroaryl optionally

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substituted by one or more  $R^8$ , het<sup>1</sup> optionally substituted by one or more  $R^8$ ,  $-S(O)_2-CH_3$ , or phenyl optionally substituted by one or more of  $NO_2$ , Cl, F,  $-OCH_3$ , and  $-OCF_3$ .

4. (Previously Presented) The method of claim 20, wherein each  $R^3$  is H.
5. (Previously Presented) The method of claim 20, wherein  $R^1$  is  $-C(O)R^6$ .
6. (Previously Presented) The method of claim 20, wherein  $R^2$  is  $-C(O)R^7$ .
7. (Previously Presented) The method of claim 6, wherein  $R^1$  is  $-C(O)R^6$ .
8. (Previously Presented) The method of claim 7, wherein  $R^6$  and  $R^7$  form  $-N(R^{17})-C(O)-N(R^{17})-$  or  $-N(R^{17})-C(S)-N(R^{17})-$ .
9. (Canceled)
10. (Canceled)
11. (Currently Amended) The method of claim 20, wherein each  $R^{15}$  is independently H, or  $C_{1-7}$  alkyl optionally substituted by one or more  $R^{11}$  substituents.
12. (Previously Presented) The method of claim 11, wherein X is  $-C(H)(C_{1-4}$  alkyl)-O-C(H)( $C_{1-4}$  alkyl)-.
13. (Currently Amended) The method of claim 20, wherein the compound has the formula of



and each  $R_{15}$  is independently (b), (c), (d), (e), (f),

or (g)

\_\_\_\_\_ (b) OR<sup>11</sup>,  
 \_\_\_\_\_ (c) Oxo,

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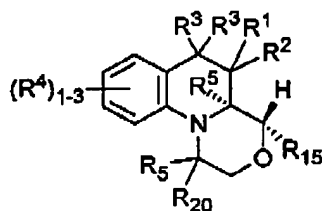
(d) C<sub>1-7</sub> alkyl which is optionally substituted by one or more R<sup>11</sup> substituents,

(e) C<sub>3-8</sub> cycloalkyl, C<sub>3-8</sub> cycloalkenyl or C<sub>3-8</sub> cycloalkynyl each of which is optionally substituted by one or more R<sup>11</sup> substituents,

(f) aryl optionally substituted by one or more R<sup>8</sup>, or

(g) heteroaryl optionally substituted by one or more R<sup>8</sup>.

14. (Currently Amended) The method of claim 20, wherein the compound has the formula of



and each R<sub>15</sub> is independently ~~(b), (e), (d), (e), (f),~~

~~or (g)~~

(b) OR<sup>11</sup>

(c) Oxo,

(d) C<sub>1-7</sub> alkyl which is optionally substituted by one or more R<sup>11</sup>

substituents,

(e) C<sub>3-8</sub> cycloalkyl, C<sub>3-8</sub> cycloalkenyl or C<sub>3-8</sub> cycloalkynyl each of which is optionally substituted by one or more R<sup>11</sup> substituents,

(f) aryl optionally substituted by one or more R<sup>8</sup>, or

(g) heteroaryl optionally substituted by one or more R<sup>8</sup>.

15. (Previously Presented) The method of claim 20, wherein R<sup>16</sup> is (C=O)OR<sup>13</sup> or C<sub>1-7</sub> alkyl.

16. (Previously Presented) The method of claim 20, wherein each R<sup>5</sup> is independently H or C<sub>1-7</sub>alkyl.

17. (Previously Presented) The method of claim 20 wherein the compound comprises

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(2R,4S,4aS)-2,4-dimethyl-8-nitro-1,2,4,4a-tetrahydro-2H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6' (1'H,3'H)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2'H)-pyrimidine]-2',4',6' (1'H,3'H)-trione;

8-Bromo-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2'H)-pyrimidine]-2',4',6' (1'H,3'H)-trione;

8-Fluoro-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2'H)-pyrimidine]-2',4',6' (1'H,3'H)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-trifluoromethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2'H)-pyrimidine]-2',4',6' (1'H,3'H)-trione;

1,1',2,3',4,4',4a,6'-Octahydro-2,4',6'-trioxospiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2'H)-pyrimidine]-8-carbonitrile;

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-carboxamidespiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2'H)-pyrimidine]-2',4',6' (1'H,3'H)-trione;

1,2,4,4a-Tetrahydro-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2'H)-pyrimidine]-2',4',6' (1'H,3'H)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2'H)-pyrimidine]-2',4',6' (1'H,3'H)-trione;

1,2,4,4a-Tetrahydro-1,4a-dimethyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2'H)-pyrimidine]-2',4',6' (1'H,3'H)-trione;

8-Bromo-1,2,4,4a-tetrahydro-cis-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2'H)-pyrimidine]-4'-thioxo-2',6' (1'H,3'H)-dione;

8-Bromo-1,2,4,4a-tetrahydro-cis-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2'H)-pyrimidine]-2',4',6' (1' methyl, 3' methyl)-trione;

*N*-[1,1',2,3',4,4',4a,6'-Octahydro-2,4-dimethyl-2',4',6'-trioxospiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5' (2'H)-pyrimidin]-8-yl]acetamide;

*tert*-butyl 1,1',2,3',4,4',4a,6'-Octahydro-2,4-dimethyl-2',4',6'-trioxospiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5' (2'H)-pyrimidin]-8-ylcarbamate;

8-Amino-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5' (2'H)-pyrimidine]-2',4',6' (1'H,3'H)-trione monohydrochloride;

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9-Bromo-1,2,4,4a-tetrahydro-2,4-dimethyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*), 5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

8-Acetyl-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

8-Ethanone-O-methyloxime-1-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-(methylsulfonyl)spiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-(methylsulfinyl)spiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-(methylthio)spiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-9-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*methyl*,3'*methyl*)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*, 3'*methyl*)-trione;

1,2, 4,4a-Tetrahydro-4-methyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-2-methyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*s*)-trione;

1,1',2'3'4'4'-Hexahydro-2',4'-dimethyl-1,3-dioxospiro[2*H*-indene-2,5'(6'*H*)-[1,4]oxazino[4,3-*a*]quinoline]-8'-carbonitrile;

1,2,4,4a-Tetrahydro-2,4-dimethyl[1,4]oxazino[4,3-*a*]quinoline-5,5,8(6*H*)-tricarbonitrile;

8-Bromo-1,2,4-4a-tetrahydro-2,4-dimethyl[1,4]oxazino[4,3-*a*]quinoline-5,5(6*H*)-dicarbonitrile;

9-(4-Chlorophenyl)-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-*a*]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

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1,2,4,4a-Tetrahydro-2,4-dimethyl-9-[4-(trifluoromethoxy)phenyl]  
spiro[[1,4]oxazino[4,3-*a*]quinoline-5(6*H*),5'(2'*H*)pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-9-(methoxyphenyl)-2,4-dimethylspiro[[1,4]oxazino[4,3-*a*]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

9-(3-Chloro-4-fluorophenyl)-1,2,4,4a,-tetrahydro-2,4-  
dimethylsprio[[1,4]oxazino[4,3-*a*]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-  
2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-9-(3-nitrophenyl)spiro[[1,4]oxazino[4,3-*a*]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)trione;

1,1',2,3',4,4',4a,6'-Octahydro-2,4-dimethyl-2',4',6'-  
trioxospiro[[1,4]oxazino[4,3-*a*]quinoline-5(6*H*),5(2'*H*)-pyrimidin]-9-yl]benzonitrile;

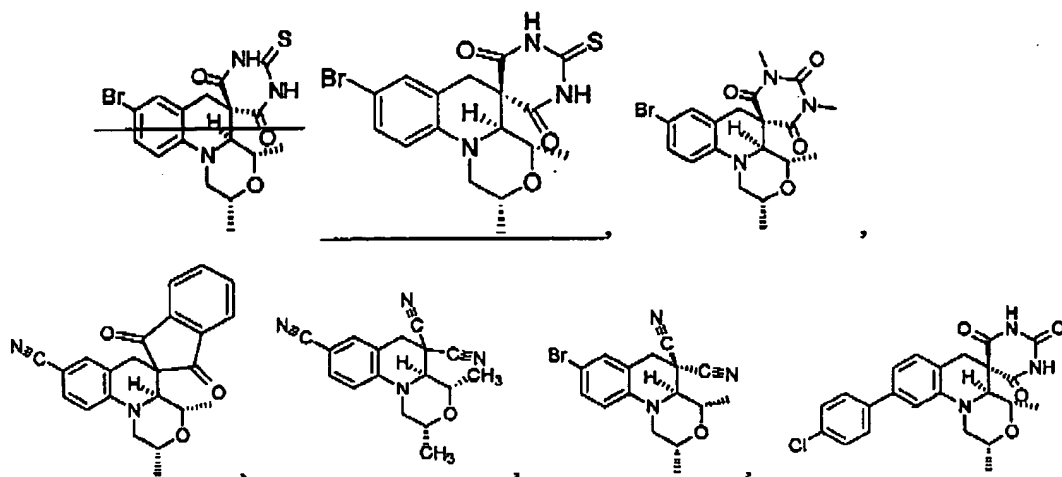
1,2,4,4a-Tetrahydro-2,4-dimethyl-9-[4-(methylsulfonyl)phenyl]  
spiro[[1,4]oxazino[4,3-*a*]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-9-(4-pyridinyl)spiro[[1,4]oxazino[4,3-*a*]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(*H*,3'*H*)-trione;

Methyl-1,1'-2,3',4,4a,6'-Octahydro-2,4-dimethyl-2',4',6'-  
trioxospiro[[1,4]oxazino [4,3-*a*]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-9-carboxylate; or

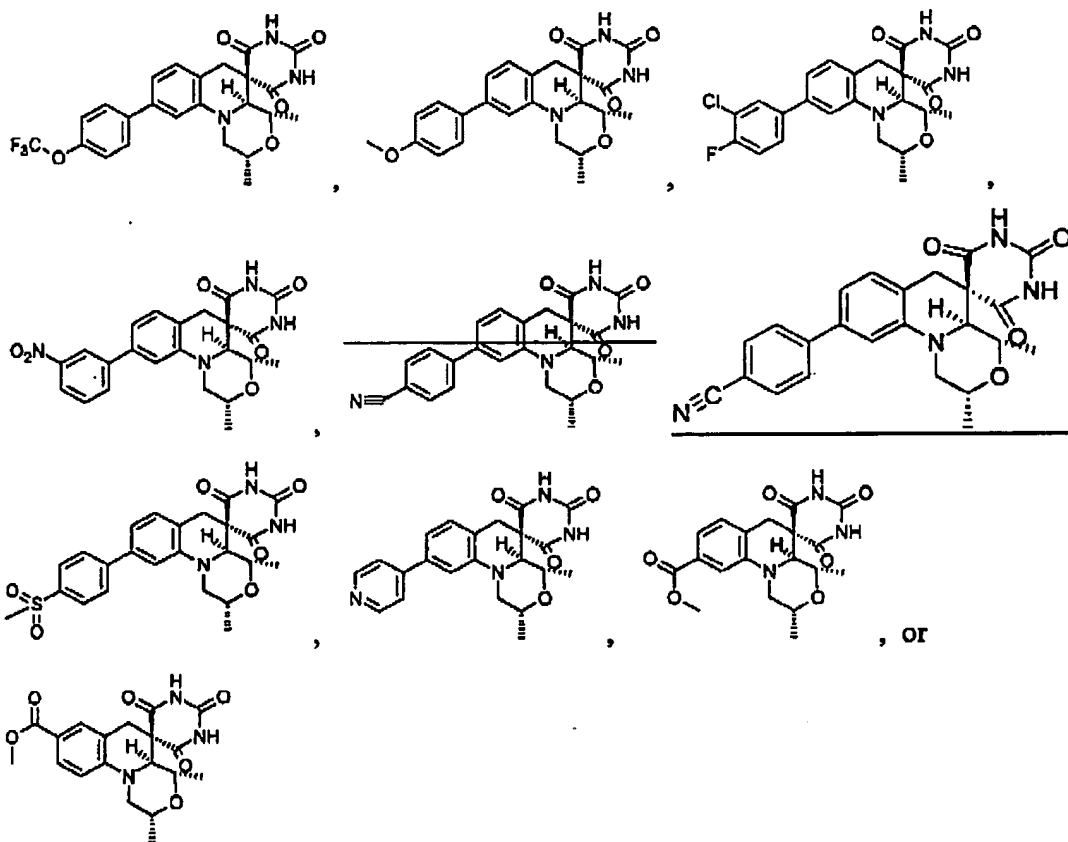
Methyl-1,1'-2,3',4,4a,6'-Octahydro-2,4-dimethyl-2',4',6'-  
trioxospiro[[1,4]oxazino [4,3-*a*]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-8-carboxylate.

18. (Previously Presented) The method of claim 20 wherein the compound  
comprises



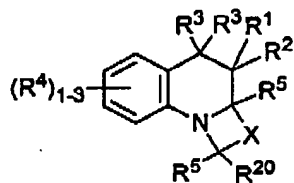
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19. (Canceled)

20. (Currently Amended) A method for the treatment of bacterial infections in mammals comprising administration of an effective amount of a compound of formula I, including enantiomeric, diastereomeric, or tautomeric isomers thereof, or any pharmaceutically acceptable salt thereof to said mammal;



I

wherein,

R<sup>1</sup> is

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- $R^2$  is
- (a)  $R^{12}$
  - (b)  $C(=O)R^6$ , or
  - (c)  $CN$ ;
- $R^2$  is
- (a)  $R^{12}$
  - (b)  $C(=O)R^7$ ,
  - (c)  $CN$ ,
  - (d)  $-CH_2-R^7$ ,
  - (e)  $-NR^{17}R^7$ ,
  - (f)  $-CH_2COR^7$ , or
  - (g)  $-CH_2CH_2COR^7$ ;

Each  $R^3$  is independently

- (a)  $H$ ,
- (b)  $R^{12}$ ,
- (c)  $C_{1-7}$  alkyl,  $C_{1-7}$  alkenyl or  $C_{1-7}$  alkynyl each of which is optionally substituted by one or more  $R^{11}$ ,
- (d)  $C_{3-8}$  cycloalkyl,  $C_{3-8}$  cycloalkenyl or  $C_{3-8}$  cycloalkynyl each of which is optionally substituted by one or more  $R^{11}$ ,
- (e) aryl optionally substituted by one or more  $R^8$ ,
- (f) heteroaryl optionally substituted by one or more  $R^8$ ,
- (g) halo, or
- (h) both  $R_3$  taken together are oxo;

Each  $R^4$  is independently

- (a)  $H$ ,
- (b) halo,
- (c)  $OR^{12}$ ,
- (d)  $OC(=O)NR^9R^{10}$ ,
- (e)  $SR^{12}$ ,
- (f)  $S(O)_mR^{13}$ ,
- (g)  $NR^9R^{10}$ ,
- (h)  $NR^9S(O)_mR^{13}$ ,



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- (i)  $\text{NR}^9\text{C}(=\text{O})\text{OR}^{13}$ ,
- (j) phenyl optionally substituted by one or more  $\text{R}^8$ ,
- (k) heteroaryl optionally substituted by one or more  $\text{R}^8$ ,
- (l) cyano,
- (m) nitro,
- (n)  $\text{CONR}^9\text{R}^{10}$ ,
- (o)  $\text{CO}_2\text{R}^{12}$ ,
- (p)  $\text{C}(=\text{O})\text{R}^{13}$ ,
- (q)  $\text{C}(=\text{NOR}^{12})\text{R}^{13}$ ,
- (r)  $\text{S}(\text{O})_m\text{NR}^9\text{R}^{10}$ ,
- (s)  $\text{NR}^9\text{C}(=\text{O})-\text{R}^{12}$ ,
- (t)  $\text{C}_{1-7}$  alkyl,  $\text{C}_{1-7}$  alkenyl or  $\text{C}_{1-7}$  alkynyl each of which is optionally substituted by one or more  $\text{R}^{11}$ ,
- (u)  $\text{C}_{3-8}$  cycloalkyl,  $\text{C}_{3-8}$  cycloalkenyl or  $\text{C}_{3-8}$  cycloalkynyl each of which is optionally substituted by one or more  $\text{R}^{11}$ ,
- (v)  $\text{N}_3$ ,
- (w)  $\text{het}^1$  optionally substituted by one or more  $\text{R}^8$ , or
- (x)  $\text{C}(\text{O})\text{O}-\text{C}_{1-4}\text{alkyl}-\text{R}^{12}$ ;

Each  $\text{R}^5$  is independently,

- (a) H,
- (b)  $\text{C}_{1-7}$  alkyl,  $\text{C}_{1-7}$  alkenyl or  $\text{C}_{1-7}$  alkynyl each of which is optionally substituted by one or more  $\text{R}^{11}$ ,
- (c)  $\text{C}_{3-8}$  cycloalkyl,  $\text{C}_{3-8}$  cycloalkenyl or  $\text{C}_{3-8}$  cycloalkynyl each of which is optionally substituted by one or more  $\text{R}^{11}$ ,
- (d) aryl optionally substituted by one or more  $\text{R}^8$ , or
- (e) heteroaryl optionally substituted by one or more  $\text{R}^8$ ;

$\text{R}^6$  and  $\text{R}^7$  are independently;

- (a)  $\text{OR}^{12}$ ,
- (b)  $\text{NR}^9\text{R}^{10}$ ,
- (c)  $\text{R}^{13}$ , or

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(e)  $R^6$  and  $R^7$  together with the 2 carbons to which they are attached form cyclohexane-1,3-dione optionally substituted by one or more  $R^{13}$ , cyclopentane-1,3-dione optionally substituted by one or more  $R^{13}$ ,  $R^6$  and  $R^7$  together form  $-N(R^{17})-S(O)_m-N(R^{17})-$ ,  $-N(R^{17})-C(O)-N(R^{17})-$ ,  $-N(R^{17})-C(S)-N(R^{17})-$ ,  $-N(R^{17})-N(R^{17})-$ ,  $-N(R^{17})-C(O)-$ , or  $-N(R^{17})-$ , or  $R^6$  and  $R^7$  together form a phenyl ring;

$R^8$  is

- (a) H,
- (b) halo,
- (c)  $OR^{12}$ ,
- (d)  $OCF_3$ ,
- (e)  $SR^{12}$ ,
- (f)  $S(O)_mR^{13}$ ,
- (g)  $NR^9R^{10}$ ,
- (h)  $NR^9S(O)_mR^{13}$ ,
- (i)  $NR^9C(=O)OR^{13}$ ,
- (j) phenyl optionally substituted by halo, cyano,  $C_{1-7}$ alkyl, or  $C_1$ .

alkoxy, in the alkyl portion of the  $C_{1-7}$ alkyl and  $C_{1-7}$ alkoxy is optionally substituted by one or more  $R^{11}$ ;

- (k) heteroaryl optionally substituted by halo,  $C_{1-7}$ alkyl, or  $C_{1-7}$ alkoxy,
- (l) cyano,
- (m) nitro,
- (n)  $CONR^9R^{10}$ ,
- (o)  $CO_2R^{12}$ ,
- (p)  $C(=O)R^{13}$ ,
- (q)  $C(=NOR^{12})R^{13}$ ,
- (r)  $S(O)_mNR^9R^{10}$ ,
- (s)  $NR^9C(=O)-R^{12}$ ,
- (t)  $C_{1-7}$ alkyl,  $C_{1-7}$ alkenyl or  $C_{1-7}$ alkynyl each of which is optionally

substituted by one or more  $R^{11}$ ,

(u)  $C_{3-8}$ cycloalkyl,  $C_{3-8}$ cycloalkenyl or  $C_{3-8}$ cycloalkynyl each of which is optionally substituted by one or more  $R^{11}$ ,

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(v) -C(O)H, or

(w) -het<sup>1</sup>;R<sup>9</sup> and R<sup>10</sup> are independently

(a) H,

(b) OR<sup>12</sup>,(c) aryl optionally substituted by one or more R<sup>14</sup>,(d) heteroaryl optionally substituted by one or more R<sup>14</sup>,(e) C<sub>1-7</sub>alkyl which is optionally substituted by one or more R<sup>11</sup>,(f) C<sub>3-8</sub>cycloalkyl which is optionally substituted by one or more R<sup>11</sup>,(g) (C=O)R<sup>13</sup>, or(h) R<sup>9</sup> and R<sup>10</sup> together with the nitrogen to which they are attached

form morpholine, pyrrolidine, piperidine, thiazine, piperazine, each of the morpholine, pyrrolidine, piperidine, thiazine, piperazine being optionally substituted with R<sup>11</sup>;

R<sup>11</sup> is

(a) oxo,

(b) phenyl optionally substituted by one or more R<sup>14</sup>,(c) OR<sup>12</sup>,(d) SR<sup>12</sup>,(e) NR<sup>12</sup>R<sup>12</sup>,

(f) halo,

(g) CO<sub>2</sub>R<sup>12</sup>,(h) CONR<sup>12</sup>R<sup>12</sup>,

(i) C<sub>1-7</sub> alkyl, C<sub>1-7</sub> alkenyl or C<sub>1-7</sub> alkynyl each of which is optionally substituted by one or more oxo, halo, OR<sup>12</sup>, SR<sup>12</sup>, C<sub>1-7</sub>alkyl, or NR<sup>12</sup>R<sup>12</sup> substituents, or

(j) C<sub>3-8</sub> cycloalkyl, C<sub>3-8</sub> cycloalkenyl or C<sub>3-8</sub> cycloalkynyl each of which is optionally substituted by one or more oxo, halo, OR<sup>12</sup>, SR<sup>12</sup>, C<sub>1-7</sub>alkyl, or NR<sup>12</sup>R<sup>12</sup> substituents;

R<sup>12</sup> is

(a) H,

(b) C<sub>1-7</sub> alkyl, C<sub>1-7</sub> alkenyl or C<sub>1-7</sub> alkynyl each of which is optionally substituted by oxo, halo, C<sub>1-7</sub>alkyl, or C<sub>1-7</sub>alkoxy substituents,

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(c) C<sub>3-8</sub> cycloalkyl, C<sub>3-8</sub> cycloalkenyl or C<sub>3-8</sub> cycloalkynyl each of which is optionally substituted by one or more oxo, halo, C<sub>1-7</sub>alkyl, or C<sub>1-7</sub>alkoxy substituents,

(d) aryl optionally substituted by one or more halo, C<sub>1-7</sub>alkyl, or C<sub>1-7</sub>alkoxy substituents, or

(e) heteroaryl optionally substituted by one or more halo, C<sub>1-7</sub>alkyl, or C<sub>1-7</sub>alkoxy substituents;

R<sup>13</sup> is

(a) C<sub>1-7</sub> alkyl which is optionally substituted by one or more by oxo, halo, carboxyl, C<sub>1-7</sub>alkyl, or C<sub>1-7</sub>alkoxy substituents,

(b) C<sub>3-8</sub> cycloalkyl, C<sub>3-8</sub> cycloalkenyl or C<sub>3-8</sub> cycloalkynyl each of which is optionally substituted by one or more by oxo, halo, C<sub>1-7</sub>alkyl, or C<sub>1-7</sub>alkoxy substituents,

(c) aryl optionally substituted by one or more halo, C<sub>1-7</sub>alkyl, or C<sub>1-7</sub>alkoxy substituents;

(d) heteroaryl optionally substituted by one or more halo, C<sub>1-7</sub>alkyl, or C<sub>1-7</sub>alkoxy substituents, or

(e) -C(O)OH

R<sup>14</sup> is

(a) H,

(b) halo,

(c) C<sub>1-7</sub>alkyl,

(d) OR<sup>12</sup>,

(e) OCF<sub>3</sub>,

(f) SR<sup>12</sup>,

(g) S(O)<sub>m</sub>R<sup>13</sup>,

(h) NR<sup>12</sup>R<sup>12</sup>,

(i) NR<sup>12</sup>S(O)<sub>m</sub>R<sup>13</sup>,

(j) NR<sup>12</sup>C(=O)OR<sup>13</sup>,

(k) phenyl optionally substituted by halo, C<sub>1-7</sub>alkyl, or C<sub>1-7</sub>alkoxy,

(l) heteroaryl optionally substituted by halo, C<sub>1-7</sub>alkyl, or C<sub>1-7</sub>alkoxy,

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- (m) cyano,
- (n) nitro,
- (o)  $\text{CONR}^{12}\text{R}^{12}$ ,
- (p)  $\text{CO}_2\text{R}^{12}$ ,
- (q)  $\text{C}(=\text{O})\text{R}^{13}$ ,
- (r)  $\text{C}(=\text{NOR}^{12})\text{R}^{13}$ ,
- (s)  $\text{S}(\text{O})_m\text{NR}^{12}\text{R}^{12}$ ,
- (t)  $\text{NR}^9\text{C}(=\text{O})\text{-R}^{12}$ ,
- (u)  $\text{C}_{1-7}$  alkyl,  $\text{C}_{1-7}$  alkenyl or  $\text{C}_{1-7}$  alkynyl each of which is optionally substituted by oxo, halo,  $\text{OR}^{12}$ ,  $\text{SR}^{12}$ ,  $\text{C}_{1-7}$ alkyl, or  $\text{NR}^{12}\text{R}^{12}$  substituents, or
- (v)  $\text{C}_{3-8}$  cycloalkyl,  $\text{C}_{3-8}$  cycloalkenyl or  $\text{C}_{3-8}$  cycloalkynyl each of which is optionally substituted by oxo, halo,  $\text{OR}^{12}$ ,  $\text{SR}^{12}$ ,  $\text{C}_{1-7}$ alkyl, or  $\text{NR}^{12}\text{R}^{12}$  substituents;

X is  $-\text{C}(\text{R}^{15})_2-\text{O}-\text{C}(\text{R}^{15})_2-$ ;

Each  $\text{R}^{15}$  is independently

- (a) H,
- (b)  $\text{OR}^{11}$ ,
- (c) Oxo,
- (d)  $\text{C}_{1-7}$  alkyl which is optionally substituted by one or more  $\text{R}^{11}$  substituents,
- (e)  $\text{C}_{3-8}$  cycloalkyl,  $\text{C}_{3-8}$  cycloalkenyl or  $\text{C}_{3-8}$  cycloalkynyl each of which is optionally substituted by one or more  $\text{R}^{11}$  substituents,
- (f) aryl optionally substituted by one or more  $\text{R}^8$ , or
- (g) heteroaryl optionally substituted by one or more  $\text{R}^8$ ;

$\text{R}^{16}$  is

- (a) H
- (b)  $\text{OR}^{12}$ ,
- (c)  $\text{C}(=\text{O})\text{R}^{13}$ ,
- (d)  $\text{C}(=\text{O})\text{OR}^{13}$ ,
- (e)  $\text{C}(=\text{O})\text{NR}^9\text{R}^{10}$ ,
- (f)  $\text{S}(\text{O})_m\text{R}^{13}$ ,

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(g)  $S(O)_mNR^9R^{10}$ ,

(h)  $C_{1-7}$  alkyl which is optionally substituted by one or more  $R^{11}$  substituents,

(i)  $C_{3-8}$  cycloalkyl,  $C_{3-8}$  cycloalkenyl or  $C_{3-8}$  cycloalkynyl each of which is optionally substituted by one or more  $R^{11}$  substituents,

(j) aryl optionally substituted by one or more  $R^8$ , or(k) heteroaryl optionally substituted by one or more  $R^8$ ; $R^{17}$  is

(a) H,

(b) -OH, or

(c)  $C_{1-4}$ alkyl; $R^{19}$  is

(a) H,

(b)  $OR^{11}$ ,

(c) Oxo,

(d)  $C_{1-7}$  alkyl which is optionally substituted by one or more  $R^{11}$  substituents,

(e)  $C_{3-8}$  cycloalkyl,  $C_{3-8}$  cycloalkenyl or  $C_{3-8}$  cycloalkynyl each of which is optionally substituted by one or more  $R^{11}$  substituents,

(f) aryl optionally substituted by one or more  $R^8$ , or(g) heteroaryl optionally substituted by one or more  $R^8$ ; $R^{20}$  is

(a) H,

(b)  $C_{1-7}$  alkyl,  $C_{1-7}$  alkenyl or  $C_{1-7}$  alkynyl each of which is optionally substituted by one or more  $R^{11}$ ,

(c)  $C_{3-8}$  cycloalkyl,  $C_{3-8}$  cycloalkenyl or  $C_{3-8}$  cycloalkynyl each of which is optionally substituted by one or more  $R^{11}$ ,

(d) aryl optionally substituted by one or more  $R^8$ ,(e) heteroaryl optionally substituted by one or more  $R^8$ , or(f)  $R^{20}$  and  $R^{19}$ , taken together, form  $-CH_2-$ ;

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wherein, "aryl" denotes a phenyl radical or an ortho-fused bicyclic carbocyclic radical having about nine to ten ring atoms in which at least one ring is aromatic;

wherein, "heteroaryl" encompasses a radical attached via a ring carbon or ring nitrogen of a monocyclic aromatic ring containing five or six ring atoms consisting of carbon and 1, 2, 3, or 4 heteroatoms, selected from oxygen (-O-), sulfur (-S-), ~~oxygenated sulfur such as sulfinyl (S=O) and sulfonyl (S(=O)<sub>2</sub>)~~, or nitrogen N(Z) wherein Z is absent or is H, O, C<sub>1-4</sub>alkyl, phenyl or benzyl, or a radical of an ortho-fused bicyclic heterocycle of about eight to ten ring atoms derived therefrom;

het<sup>1</sup> is a C- or N- linked five- (5), six- (6), seven- (7), or eight- (8) membered mono- or bicyclic ring, each mono- or bicyclic ring being fully saturated or partially unsaturated, and having 1-4 heteroatoms selected from the group consisting of oxygen, sulfur, and nitrogen; het<sup>1</sup> being optionally substituted by 1-2 substituents selected from C<sub>1</sub>-C<sub>4</sub>alkyl, amino, C<sub>1</sub>-C<sub>4</sub>alkylamino, C<sub>1</sub>-C<sub>4</sub>alkyloxy, halogen -CN, =O, and =S;

each m is independently 0, 1, or 2; and

each n is independently 1, 2, or 3.

21. (Previously Presented) The method of claim 20 wherein said compound is administered to the mammal orally, parenterally, transdermally, or topically in a pharmaceutical composition.

22. (Original) The method of claim 20 wherein said compound is administered in an amount of from about 0.1 to about 100 mg/kg of body weight/day.

23. (Original) The method of claim 20 wherein said compound is administered in an amount of from about 1 to about 50 mg/kg of body weight/day.

24. (Canceled)

25. (Canceled)

26. (Previously Presented) The method of claim 20 wherein the composition comprises an enantiomerically enriched form of a compound of formula I.

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27. (Previously Presented) The method of claim 26, wherein the composition comprises at least 50% of one enantiomer of a compound of formula I relative to the other enantiomer of the compound.

28. (Previously Presented) The method of claim 27, wherein the composition comprises at least 80% of one enantiomer of a compound of formula I relative to the other enantiomer of the compound.

29. (Previously Presented) The method of claim 27, wherein the composition comprises at least 90% of one enantiomer of a compound of formula I relative to the other enantiomer of the compound.

30. (Previously Presented) The method of claim 20 wherein the compound comprises

(2S,4R,4aR)-4-isopropyl-2-methyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

(2R,4S,4aS)-2,4-diethyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

(2R,4S,4aS)-2,4-dimethyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

(2R,4S,4aS)-8-acetyl-9,10-difluoro-2,4-dimethyl-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

(2R,4S,4aS)-10-fluoro-2,4-dimethyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

(2R,4S,4aS)-2,4-dimethyl-8-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione;

(2S,4R,4aR)-2-isopropyl-4-methyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;



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(2S,4R,4aR)-2-isopropyl-4-methyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

(2R,4S,4aS)-2,4-diisopropyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

(2R,4S,4aS)-2,4-dimethyl-8-(3-methyl-1,2,4-oxadiazol-5-yl)-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

(2S,4R,4aR)-8-aceryl-10-fluoro-2,4-dimethyl-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

8-bromo-2,4-dimethyl-10-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

(2R,4S,4aS)-2,4-dimethyl-8-(5-methyl-1,2,4-oxadiazol-3-yl)-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

(2S,4S,4aS)-4-methyl-8-nitro-2-(trifluoromethyl)-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

4-azido-3-iodobenzyl (2R,4S,4aS)-2,4-dimethyl-2',4',6'-trioxo-1,1',2,3',4,4',4a,6'-octahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-8-carboxylate; or

(2S,4S,4aS)-2,4-dimethyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione.

31. (Previously Presented) The method of claim 20 wherein:

when each R<sub>4</sub> is H, that R<sub>1</sub> and R<sub>2</sub> are not simultaneously H, CN, or -C(O)-OCH<sub>3</sub> or that R<sub>1</sub> is not CN and R<sub>2</sub> is not -C(O)-OC<sub>1-4</sub>alkyl;

when the compound is 1,2,4,4a-Tetrahydro-cis-2,4-dimethyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione that the compound is enantiomerically enriched (-) form of (2R,4S,4aS)-2,4-dimethyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione.

32. (Previously Presented) The method of claim 20 wherein the compound of formula I is administered as a pharmaceutical composition, wherein the pharmaceutical composition additionally comprises a pharmaceutically acceptable carrier.

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33. (Previously Presented) The method of claim 4 wherein:

$R^1$  is  $-C(O)R^6$ ;

$R^2$  is  $-C(O)R^7$ ;

each  $R^4$  is independently selected from H, F and heteroaryl optionally substituted by one or more  $R^8$ ;

each  $R^5$  is H;

$R^6$  and  $R^7$  form  $-N(R^{17})-C(O)-N(R^{17})-$ ;

each  $R^{17}$  is H;

$R^{20}$  is H; and

X is  $-C(H)(C_{1-4} \text{ alkyl})-O-C(H)(C_{1-4} \text{ alkyl})-$ .

34. (Previously Presented) The method of claim 33 wherein  $R^8$  is  $C_{1-7}$  alkyl.

35. (Previously Presented) The method of claim 13 wherein:

$R^1$  is  $-C(O)R^6$ ;

$R^2$  is  $-C(O)R^7$ ;

each  $R^3$  is H;

each  $R^4$  is independently selected from H, F and heteroaryl optionally substituted by one or more  $R^8$ ;

each  $R^5$  is H;

$R^6$  and  $R^7$  form  $-N(R^{17})-C(O)-N(R^{17})-$ ;

each  $R^{15}$  is  $C_{1-7}$  alkyl;

each  $R^{17}$  is H; and

$R^{20}$  is H.

36. (Previously Presented) The method of claim 35 wherein  $R^8$  is  $C_{1-7}$  alkyl.